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Prognosis and Treatment of Liver Transplant Recipients in the COVID-19 Era: A Literature Review

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Liver transplantation during the COVID-19 pandemic is challenging. Both donor and recipient issues can be influenced by the risks attributed to the pandemic. Allocation policy may need to be modified and criteria may be influenced by local infection rates and availability of medical facilities. Modifying immunosuppression (IS) protocols is controversial and is not evidence-based. In this study, we review the published literature on liver transplant recipients who were infected with COVID-19.

A literature review was performed using PubMed, ScienceDirect, and WHO databases to identify relevant English-language articles published up to May 20, 2020.

Fifteen articles reported 120 liver transplant recipients who were infected with COVID-19. Only 10 papers with 22 patients reported full encounter characteristics. Four papers reported 23, 17, 13, and 6 patients, respectively, but with minimal data. One paper reported the authors' own 39 patients' characteristics and demographics. The mean age was 58.2 years with 66% males. The most commonly reported presentations in descending order were fever (91%), cough (36.7%), shortness of breath (SOB) (31.8%), and diarrhea (31.8%). Liver transplant patients infected with COVID-19 were maintained on Tac (79%), mycophenolate (MMF) (48.4%), and Prednisone (29.6%) and were managed by reducing MMF in 14.3% of patients and reducing Tac in 14.3% of patients; 28.6% of patients needed ICU admission, 13.6% of patients had died, and the reported general population COVID-19 mortality rate was 3.4%.

The clinical presentation of COVID-19 in liver transplant recipients may be different from the general population, with higher rates of severe disease, complications, and mortality.

MeSH Keywords: COVID-19 • Liver Transplantation • Organ Transplantation • SARS Virus

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Background

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV2) [1]. The disease was initially confirmed in China and then rapidly spread worldwide with more than 4.8 million infected individuals and over 300 000 deaths worldwide [2]. This disease is especially deadly in elderly patients (over 70 years old) with comorbidities [3]. Most published data regarding COVID-19 and organ transplant recipients are nonspecific and lack quality evidence. Data on demographics, characteristics, and clinical presentations of COVID-19 in organ transplant recipients are scarce. In the present study, we review the published literature regarding liver transplant patients who were infected with COVID-19.

Material and Methods

Literature Search

A systematic literature review was performed using PubMed and ScienceDirect databases to identify relevant English-language articles published through May 20, 2020. Search terms were COVID-19, coronavirus, severe acute respiratory syndrome coronavirus 2, 2019-nCoV, SARS-CoV-2, SARS-CoV, MERS-CoV, liver transplantation, and liver transplant. All article types were included: case reports, case series, commentaries, and review articles. A search in the database of the COVID-19 Global Research on Coronavirus Disease section of the WHO website through May 20, 2020 was performed using the following criteria: liver transplantation or liver transplant with English language as limit or filter [4]. Additional articles were retrieved by screening the reference lists of the included studies. The search strategy was approved and reviewed by all authors.

Eligibility criteria and study selection

The authors independently reviewed the titles and abstracts for inclusion. Figure 1 displays the flow diagram for this systematic review, based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 [5]. Databases were screened, filtered, and assessed for eligibility. Cases of COVID-19 in liver transplant patients were included in this study. Articles with unrelated topics and/or with missed information were excluded.

Risk of bias

The National Institutes of Health Quality Assessment Tool for Case Series Studies was used to qualify the reviewed articles [6]. Table 1 shows the results of the 2 reviewers who independently rated the quality of the included studies.

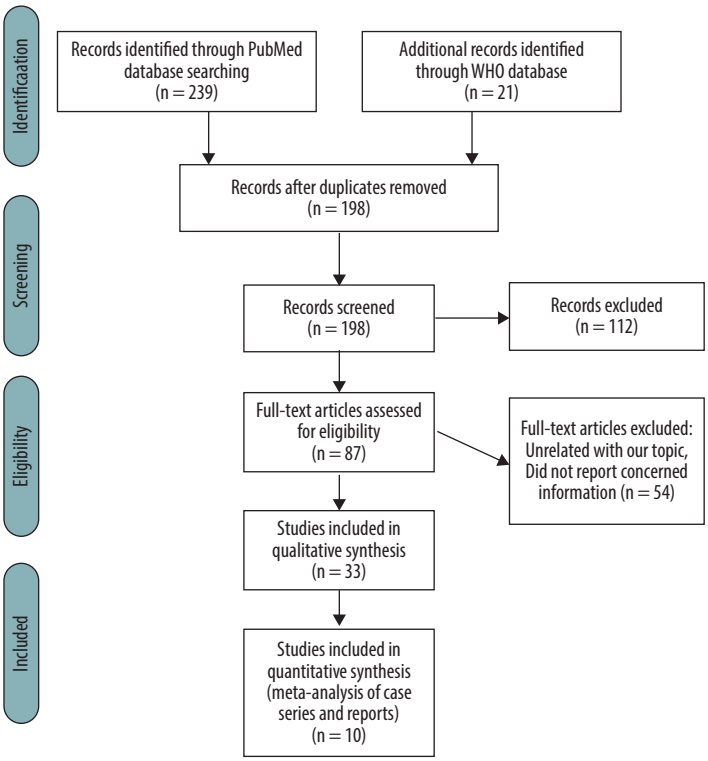

Figure 1. PRISMA flow chart for the present study.

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Table 1. Quality ratings of included studies according to NIH Quality Assessment Tool for case series studies.

Study	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q 8	Q 9	Reviewer 1	Reviewer 2
Zhong	Yes	No	CD	Yes	CD	Yes	No	Yes	Yes	Fair	Fair
Liu	Yes	Yes	NA	NA	Yes	Yes	No	NA	Yes	Fair	Fair
Huang	Yes	Yes	CD	No	Yes	Yes	Yes	NA	Yes	Fair	Fair
Qin	Yes	Yes	CD	Yes	Yes	Yes	Yes	NA	Yes	Fair	Fair
Morand	Yes	Yes	NA	NA	No	Yes	No	NA	Yes	Fair	Fair
Lagana	Yes	Yes	CD	Yes	Yes	Yes	Yes	NA	No	Fair	Fair
Kates	Yes	Yes	NA	NA	Yes	Yes	Yes	NA	Yes	Fair	Fair
Hammami	Yes	Yes	NA	NA	Yes	Yes	No	NA	Yes	Fair	Fair
Fernández-Ruiz	Yes	No	NA	NA	No	Yes	No	NA	Yes	Fair	Fair
Donato	Yes	NO	CD	Yes	No	Yes	Yes	Yes	Yes	Fair	Fair

NIH – National Institutes of Health: NR – not reported: CD – cannot determine; NA – not applicable. The NIH Quality Assessment Tool for Case Series Studies poses nine questions: 1=Was the study question or objective clearly stated?, 2=Was the study population clearly and fully described, including a case definition?, 3=Were the cases consecutive?, 4=Were the subjects comparable?, 5=Was the intervention clearly described?, 6=Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?, 7=Was the length of follow-up adequate?, 8=Were the statistical methods well-described?, 9=Were the results well-described?

Data extraction and synthesis

Data were independently extracted from reports by 2 reviewers. All reported patients' demographic and clinical characteristics (country, age, sex, time from transplant, comorbidities, clinical presentation and maximum body temperature, initial laboratory values, baseline immunosuppressant medications (ISM), need for intensive care unit (ICU), duration of illness, and outcomes) were extracted, collected, and analyzed. Due to the lack of sufficient data, we did not perform a meta-analysis to assess the association of various patients' findings with demographic data, disease and patient characteristics, or outcomes. The principal summary measures used were the median, mean, standard deviation, and incidence.

Results

Overview of the included studies

A total of 260 articles were retrieved using the search strategy. After removing duplicate articles, 198 articles were screened, of which 112 articles were excluded due to unrelated content. The remaining 87 articles were assessed for eligibility through full-text screening, then 54 articles were excluded due to unrelated content or lack of relevant information. There were 33 articles included but only 15 articles reported liver transplant recipients infected with COVID-19 (Figure 1). Of these 15 articles, there were 2 case series and 8 case reports that reported a total of 22 liver transplant patients. Four articles reported 23, 17, 13, and 6 patients, respectively, but with minimal data [7–10]. One paper reported the authors' own 39 patients' characteristics and demographics [11] and was used in Table 2 for comparison and to extract pooled measurements. The remaining 18 articles were commentaries and review articles. Patients' characteristics and demographics were included in Tables 3–7.

Patients demographics and characteristics

Ten articles reported 22 liver transplant patients infected with COVID-19. There were 8 from Italy, 6 from Spain, 4 from China, 3 from the USA, and 1 from France. There were 15 (68.2%) males. The mean age was 55.96 (0.5–79) years. The mean post-transplant period was 8.75 (0.005–26) years, and 22.7% of patients were within the first year after transplantation. The most common reported comorbidities were diabetes mellitus in 22.7%, heart disease in 22.7%, lung disease in 22.7%, HTN in 18.2%, and obesity in 4.6%, and 40.9% of patients had no reported comorbidities.

Clinical presentation

The most frequently reported clinical presentation was fever; it was reported in 90.9%, with a mean maximum temperature of 39.26°C (±0.54). Other reported clinical symptoms were cough (36.7%), shortness of breath (31.8%), unspecified respiratory symptoms (31.8%), diarrhea (31.8%), and fatigue (27.3%). Less frequently reported symptoms included headache, dizziness, weakness, abdominal discomfort, sleep disorders, chills, rhinitis, confusion, myalgia, and chest pain.

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Table 2. Clinical characteristics of the 22 reported liver transplant patients infected with COVID-19 compared with previous published studies.

Variable	This study	Webb et al. [11]	Pooled (mean)
Number of patients	22	39	61
Age (Mean)	55.96	60.50	58.25
Sex			
Male	68.2%	64.1%	66.15%
Liver transplant years age (mean)	8.75	5.5	7.125
Comorbidities			
HTN	18.2%	46.2%	32.2%
DM	22.7%	38.5%	30.6%
Heart disease	22.7%	15.4%	19%
Obesity	4.6%	25.7%	15.15%
Baseline Immunosuppression			
Tacrolimus	68.2%	89.7%	79%
Mycophenolate mofetil	45.5%	51.3%	48.4%
Prednisone	18.2%	41%	29.6%

Laboratory results

The initial white blood cell count median was 3.2×10^3 ($\pm1.56\times10^3$). The initial median lymphocyte cell count was 0.67×10^3 ($\pm0.18\times10^3$). Initial leukopenia and lymphopenia were reported in 60% and 100%, respectively. The median initial CRP was 21.5 (±15.6) mg/L, and high CRP (>5 mg/dl) levels were noted in 75%. High ALT (>50 U/l) and AST (>54 U/l) were reported in 71.4% and 60%, respectively.

Immunosuppression management

Patients were treated with different IS regimens. Tacrolimus (Tac) was prescribed in 68.2% of patients and discontinued in 14.3%, reduced in 14.3%, and not changed in 28.6%. MMF was prescribed in 45.5% of patients and discontinued in 7.1% and reduced in 14.3%. The exact MMF management was not reported in the remaining 79% of patients. Pred was prescribed in 18.2% of patients and not changed in 50% of patients; the exact Pred management was not reported in the remaining 50% of patients. Other baseline ISMs were Azathioprine, Everolimus, and Cyclosporin. These medications were held in some patients and not changed in others; 27.2% of patients had no change in ISM and recovered.

Deceased patients were prescribed MMF in 100%, Tac in 33.3%, and EVE in 33.3% and had their ISM held (MMF 66.6%; EVE 100%) or reduced (MMF 33.3%; Tac 33.3%).

COVID-19 directed management

Treatment targeted COVID-19 included hydroxychloroquine (42.9%), antibiotics (35.7%), lopinavir/ritonavir (28.6%), INF-a,b (28.6%), intravenous methylprednisolone (21.4%), intravenous immunoglobulin (14.3%), oseltamivir (14.3%), azithromycin (7.1%), and tocilizumab (7.1%). COVID-19 targeting treatment used in patients who died included antibiotics (33.3%), hydroxychloroquine (33.3%), lopinavir/ritonavir (66.6%), INF-a,b (66.6%), and umifenovir (33.3%).

Patients outcomes

Intensive care unit (ICU) admission occurred in 28.6% of patients, 72.7% of patients had recovered and were discharged with a median illness duration of 17 days (range, 6–53 days), 13.6% of patients were alive and hospitalized at the time of publication with a median illness duration of 16 days, and 13.6% of patients had died with a median illness duration of 24 days (range, 7–45 days).

Characteristics of patients who died

The mean age of patients who dies was 68 years, 66.6% of patients were older than 65 years, 100% of patients were male, and the mean time from transplant was 8.2 years. Diabetes mellitus, hypertension (HTN), obesity, asthma, and bronchiectasis were reported in these patients; 66.6% had lymphopenia and 66.6% had high CRP serum levels. ARDS and acute renal failure were reported in 100% and 66.6% of patients, respectively.

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Table 3. Characteristics of all available reported liver transplant recipients infected with COVID-19.

Study; Country	Age	Sex	Time from transplant (years)	Comorbidities	Clinical presentation	Highest temp (°C)	Baseline ISM
Zhong; China [30]	37	M	9 days		Fever 38.6°C, Weakness, Abdominal discomfort, sleep disorders	38.6	Tac, IVMP
Liu; China [31]	50	M	2.5		Fever 37.7°C, SOB,	39.6	Tac,
Huang; China [32]	59	M	2.7		Fever 40, Cough, Chills, Fatigue, Diarrhea, Jaundice, Splenomegaly, Ascites,	40	Tac, MMF
Qin; China [33]	37	M	12 days		Fever 39,	39	Tac, Pred
Morand; France [34]	4.6	F	5 months		Fever, Cough, SOB, Rhinitis,		Tac
Lagana; USA [35]	6 months	F	2 days		Fever, SOB, Diarrhea		MMF
Kates; USA [36]	67	M	19		Fever, Cough, Fatigue, confusion, Diarrhea, Wheezing		cyclosporine
Hammami; USA [37]	63	M	9.5	HTN, DM, ESRD, PVD, CHF,	Fever 38.3, Cough, Headache, Fatigue, Myalgia, Chest pain, Chills, Abdominal pain,	39.1	Tac,
Fernández-Ruiz; Spain [38]	63	M	7.9	HTN, DM	Fever, SOB, Cough, Myalgia, Fatigue, Diarrhea		everolimus
	72	M	5.5	HTN, DM, Obesity,	Fever, SOB, Cough,		MMF, everolimus
	79	F	15.3	DM, ESRD,	SOB, Cough, Fatigue, Diarrhea		Everolimus, Pred, azathioprine
	73	M	16.4	DM, Asthma, bronchiectasis	Fever, SOB, Cough, Fatigue,		MMF
	76	F	26.5	HTN	Fever, Chest pain		Tac
	46	F	6.4		Diarrhea		Tac
Donato; Italy [39]	60	M	3		Fever, Respiratory symptoms		Tac, MMF
	78	M	19.1	Heart Disease	Fever, Respiratory symptoms		Tac, MMF
	65	M	5.4	Lung disease	Fever, Respiratory symptoms		Pred
	57	M	15.6	Heart and lung diseases	Fever, Respiratory symptoms		Tac, MMF
	57	M	8		Fever, Respiratory symptoms		Tac, MMF
	62	F	11.4	Lung disease	Fever, Respiratory symptoms		Tac, MMF
	75	M	17.6	Heart disease	Fever, Diarrhea		Tac, MMF
	50	F	3 months	Heart and lung diseases	Fever, Respiratory symptoms		Tac, Pred

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Table 4. Laboratory characteristics of all available reported liver transplant recipients infected with COVID-19.

Study	Initial bilirubin (μmol/L)	Highest bilirubin	Initial WBC	Initial LC	Initial PLT	Initial CRP	Initial AST	Highest AST	Initial ALT	Highest ALT
Zhong	38.9	103.7	2.46	0.48	74			122	240	424
Liu			5.9	0.42		32.1	N		N	
Huang	83.9	528.8	3.2	0.7		35.1			60	
Qin				0.64			132		80	
Morand						3.2	120		224	
Lagana							163	908	215	1253
Kates			1.93	0.9			39		12	
Hammami			4.1	0.77	71	11	21		17	

Table 5. Management and outcomes of all available reported liver transplant recipients infected with COVID-19.

Study	ISM management	COVID-19 targeted management	ICU	Complications	Outcome
Zhong	Tac held; IVMP	Oseltamivir, Abx,	Yes	None	Recovered, 40d
Liu	Tac held; IVMP	Umifenovir, lopinavir/ritonavir, IVIG, Abx, INF-a	No	None	Recovered, 35d
Huang	Reduced Tac, MMF; IVMP	Umifenovir, lopinavir/ritonavir, Abx, INF-a		Respiratory failure, AKI, MOF,	Died, 45d
Qin	No change	Oseltamivir, IVIG, rh-GCSF, Abx			Recovered, 53d
Morand	Reduced Tac	Paracetamol			Recovered, 11d
Lagana	Reduced MMF	Hydroxychloroquine	Yes	None	Hospitalized, 16d
Kates	No change		Yes	AKI	Recovered, 6d
Hammami	No change	Hydroxychloroquine, Azithromycin, Abx, tocilizumab			Recovered, 16d
Fernández-Ruiz	Held EVE and start Tac, MMF	Hydroxychloroquine, lopinavir/ritonavir			Recovered, 19d
	Held EVE, MMF and start Tac	Hydroxychloroquine, lopinavir/ritonavir, IFN-b		AKI, ARDS,	Died, 7d
	No change	Hydroxychloroquine, IFN-b			Recovered, 14d
	Held MMF		Yes	ARDS, Refractory shock	Died, 24d
	No change	Hydroxychloroquine			Recovered, 15d
	No change				Recovered, 18d
Donato					6 Recovered, 2 Hospitalized

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Table 6. Clinical characteristics for the 22 reported liver transplant patients infected with COVID-19.

Variable (n=22)	Value	
Age (mean, range)	55.96	(0.5–79)
Sex, Male	15/22	(68.2%)
Liver transplant years age (mean, range)	8.75	(0.005–26)
Within 1 year	5/22	(22.7%)
Beyond 1 year	17/22	(77.2%)
Comorbidities		
HTN	4/22	(18.2%)
DM	5/22	(22.7%)
Lung disease	5/22	(22.7%)
Heart disease	5/22	(22.7%)
Obesity	1/22	(4.6%)
None or N/A	9/22	(40.9%)
Clinical presentation		
Fever	20/22	(90.9%)
Max. temp (average, SD)	39.26	(±0.54)
Cough	8/22	(36.7%)
SOB	7/22	(31.8%)
Unspecified respiratory symptoms	7/22	(31.8%)
Fatigue	6/22	(27.3%)
Diarrhea	7/22	(31.8%)
Laboratory		
White cell count		
Median (SD) per l	3.2×10^9	($\pm1.56\times10^9$)
Leukopenia ($<4\times10^9$/l)	3/5	(60%)
Lymphocyte count		
Median (SD) per l	0.67×10^9	($\pm0.18\times10^9$)
Lymphopenia ($<1\times10^9$/l)	6/6	(100%)
Initial C-reactive protein (CRP)		
Median (SD)	21.5	(±15.6)
High CRP (>5 mg/dl)	3/4	(75%)
Initial ALT		
Median (SD)	80	(±101)
High ALT (>50 U/l)	5/7	(71.4%)
Initial AST		
Median (SD)	120	(±61.7)
High AST (>54 U/l)	3/5	(60%)

Pooled results

One study reported 39 patients without demographics and characteristics for each patient and these were thus not included in our tabulated results. However, the study was used to draw pooled measures for all reported liver transplant patients infected with COVID-19 in the literature. A total of 61 liver transplant patients with COVID-19 used in the comparison. The age mean was 58.25 years and 66.15% were males. The mean age at transplant was 7.13 years. HTN, DM, heart disease, and obesity were reported in 32.2%, 30.6%, 19%, and 15.1% of patients, respectively. Liver transplant patients infected with COVID-19 were maintained on Tac (79%), MMF (48.4%), and Pred (29.6%).

Discussion

Most published reports on COVID-19 in organ transplant recipients are nonspecific and lack quality evidence. Data on demographics, characteristics, and clinical presentations of COVID-19 in organ transplant recipients is scarce. However, it is well known that among patients with advanced age and medical comorbidities, COVID-19 is frequently severe. Studies have reported that COVID-19 can present differently in immunosuppressed patients, including organ transplant recipients.

Fever in COVID-19 in the general population is reported in 99% of patients [12,13]. Our study has shown that 9% of the liver transplant patients did not have fever on presentation or during their hospitalization. On the other hand, cough, SOB, myalgia, headache, sore throat, and gastrointestinal symptoms were different in incidence from the typical COVID-19 presentation [12–15]. Additionally, this review shows that there are several unreported symptoms that can appear in the COVID-19-positive liver transplant patients, including chest tightness and pain and jaundice [14]. Notably, the unreported chest tightness and pain in other cohorts have an incidence of 9% in this cohort.

COVID-19 causes pneumonia that can be severe enough to be lethal, especially in patients with advanced age or underlying

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Table 7. Management and outcomes of the 22 reported liver transplant patients infected with COVID-19.

Variable	Value
Baseline Immunosuppression	
Tacrolimus	15/22 (68.2%)
Mycophenolate mofetil	10/22 (45.5%)
Prednisone	4/22 (18.2%)
Azathioprine	1/22 (4.5%)
Everolimus	3/22 (13.6%)
Ciclosporin	1/22 (4.5%)
Management	
Immunosuppression	
Held tacrolimus	2/14 (14.3%)
Reduced tacrolimus	2/14 (14.3%)
No change tacrolimus	4/14 (28.6%)
Held mycophenolate mofetil	1/14 (7.1%)
Reduced mycophenolate mofetil	2/14 (14.3%)
Prednisone	No change 2
Azathioprine	No change 1
Everolimus	Held 2
Ciclosporin	No change 1
Other Tx	
Lopinavir/Ritonavir	4/14 (28.6%)
Hydroxychloroquine	6/14 (42.9%)
Azithromycin	1/14 (7.1%)
Oseltamivir	2/14 (14.3%)
Antibiotics	5/14 (35.7%)
Intravenous methylprednisolone	3/14 (21.4%)
Intravenous immunoglobulin	2/14 (14.3%)
Interferon a,b	4/14 (28.6%)
Tocilizumab	1/14 (7.1%)
ICU admission	4/14 (28.6%)
Outcomes	
Clinically recovered/ discharged	16/22 (72.7%)
Illness days duration (median, range)	17 (6–53)
Alive but suffers/In hospital	3/22 (13.6%)
Illness days duration (median)	16
Death	3/22 (13.6%)
Illness days duration (median, range)	24 (7–45)

medical comorbidities [16]. Those comorbidities include cardiovascular disease, diabetes mellitus, HTN, chronic lung disease, cancer, chronic kidney disease, and obesity (body mass index ≥30) [3,16]. Liver transplant patients infected with COVID-19 are a fragile and high-risk group due to immunosuppression and common comorbidities. In this review, 60% of patients had comorbidities. These comorbidities predispose these patients to a more severe COVID-19 infection. The attendant IS is an additional risk factor for severe disease. Liver transplant recipients and candidates are in a high-risk group due to the high incidence and prevalence of hypertension, renal failure, diabetes, obesity, and advanced age in this group.

It was previously reported that a progressive decline in lymphocyte count was observed in non-survivors compared to more stable levels in survivors [12]. In the present study, 100% of patients who died had lymphopenia. Given the fact that ISM can induce lymphopenia, many liver transplant patients have a baseline lymphopenia that might further deteriorate and worsen the prognosis [17,18].

Several studies and a report from the Chinese Center for Disease Control and Prevention have classified COVID-19 severity in the general population [19,20] as mild, severe, and critical disease in 81%, 14%, and 5% of patients, respectively. In this report, severe disease defined by SOB and/or hypoxemia was reported in 31.3% of patients.

The WHO reported that recovery time appears to be around 2 weeks for mild infections and 3 to 6 weeks for severe disease [21]. In the present study, we found that 72% of patients recovered clinically from the COVID-19, with a median duration of illness of 17 (6–53) days. Rates of ICU admission were reported to range between 5% and 12% in the general population [22]. In our cohort, 28.6% of patients were admitted to the ICU.

The most recently reported mortality rate of COVID-19 was 3.77% [23]. The mortality rate of liver transplant patients infected with COVID-19 in this cohort was 13.6% (3 out of 22

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patients). Despite the small number of patients included in the present study, this high mortality indicates that COVID-19 in liver transplant patients may portend an ominous outcome. Surprisingly, 17.6% of patients with time from transplant longer than 1 year had died, while there were no deaths within the first year of transplantation. This is despite the fact that the first year is fraught with postoperative complications and higher immunosuppression.

It was reported that 81% of COVID-19 patients present with mild disease and can be managed at home, and those with severe and critical COVID-19 disease should be managed with prompt hospitalization while ensuring appropriate infection control and supportive care [19,24,25]. The hospitalized patients should be managed with empiric treatment for bacterial pneumonia in selected patients, prevention of venous thromboembolism, and avoiding nebulized medications. The WHO and CDC recommend against use of systemic glucocorticoids in COVID-19 patients unless there are other indications [24,25]. To date, all suggested medications are under investigation, with no proven efficacy against COVID-19. These medications include Remdesivir, hydroxychloroquine/chloroquine, azithromycin, hydroxychloroquine, convalescent plasma, tocilizumab, favipiravir, interferon beta, and lopinavir/ritonavir. Most of our cohort were hospitalized and could not be managed at home due to the severity of the disease. They were managed with hydroxychloroquine (42.9%), antibiotics (35.7%), lopinavir/ritonavir (28.6%), INF-a,b (28.6%), intravenous methylprednisolone (21.4%), intravenous immunoglobulin (14.3%), oseltamivir (14.3%), azithromycin (7.1%), and tocilizumab (7.1%).

The effect of IS on the progression of COVID-19 is unclear. There are 2 aspects that should not be ignored when dealing with IS and COVID-19. First, it was proved that COVID-19 patients have a high prevalence of lymphopenia [26] but its unclear whether lymphopenia is a risk factor for COVID-19 or is a result of it. Second, it is thought that the severity of COVID-19 may be the result of a hyperinflammatory response (cytokine storm). Thus, the role of immunomodulation may have a positive and not just a negative effect in the treatment of severe cases [27,28].

Interestingly, a recent Italian report by Lorezo D'Antiga concluded that immunocompromised patients do not have an increased risk of developing severe pulmonary disease compared to the general population [29]. Nevertheless, it is evident from this study that liver transplant patients are at an increased risk for serious, critical, and fatal disease when infected with COVID-19.

Conclusions

Liver transplant patients may have an atypical clinical presentation of COVID-19 infection. Fever may be absent while other atypical symptoms may prevail. Therefore, a high index of suspicion for COVID-19 and perhaps even surveillance in this population may help in early diagnosis and prevention of further transmission. The role of IS therapy should be assessed in every case individually.

Conflicts of interest

None.

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